IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Turner *et al.*	Group Art Unit: 1646
Application No.:	09/658,283	Examiner: J.F. Murphy
Filed:	09/08/00	
Title:	Novel Human 7TM Proteins and Polynucleotides Encoding the Same	Att Docket No.:LEX-0041-USA

APPEAL BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
Alexandria, VA 22313

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES

APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on December 26, 2002. The Notice of Appeal was timely submitted on March 26, 2003, and was received in the Patent and Trademark Office ("the Office") on April 1, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of three months to and including September 1, 2003, which falls on a holiday and is thus extended to September 2, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(2) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief (**$160.00**), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences.

III. STATUS OF THE CLAIMS

The present application was filed on September 8, 2000, claiming the benefit of U.S. Provisional Application Numbers 60/153,366 and 60/165,510, which was filed on September 10, 1999 and November 15, 1999, respectively, and included original claims 1-6.

A Restriction and Election Requirement was issued by the Office on June 10, 2002, via telephone conference with Peter Seferian, restricting to a particular invention. In Response to the Restriction Requirement, Appellants elected, without traverse, the claims of the Group I invention (comprising original claims 1-2 and 6) for prosecution on the merits and claims 3-5 are withdrawn from further consideration by examiner, 37 CFR1.142(b), as being drawn to a non-elected invention.

A First Official Action, was issued on July 1, 2002 ("the First Action"), claims 1-2, 6 were rejected to under 35 U.S.C. § 101 as allegedly the invention lacks patentable utility, claims 1-2, 6 were also rejected under 35 U.S.C. § 112, first paragraph, allegedly the invention was unusable by the skilled artisan due to the alleged lack of patentable utility, claims 1-2 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to provide written description an enablement, claims 1-2 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and claims 1-2 were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Hillier, et al. 1996 (accession no. T71087).

In a response to the First Official Action, submitted to the Office on October 1, 2002 ("response to the First Action"), Appellants amended claims 1 and 2 to further improve their clarity, and new claim 7 was added to more particularly point out and distinctly claim the invention.

A Second and Final Official Action, was issued on December 26, 2002 ("the Final Action"), in which rejection of claims 1-2, 6 and new claim 7 was maintained under 35 U.S.C. § 101 due to an alleged lack of patentable utility, rejection of claims 1-2, 6 and new claim 7 was also maintained under 35 U.S.C. § 112, first paragraph, as one skilled in the art clearly would not know how to use the skilled invention, rejection of claim 2 was also maintained under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and the rejection of claims 1-2 under 35 U.S.C. § 102(b) was withdrawn.

In a response to the Final Action, submitted on April 28, 2003 ("response to the Final Action"), Appellants amended claim 2 and again addressed the outstanding rejections of claims 1, 2, 6 and 7.

An Advisory Action ("the Advisory Action") was mailed on August 20, 2003, maintaining the rejection of claims 1, 2, 6 and 7 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and the rejection of claims 1, 2, 6 and 7 under 35 U.S.C. § 112, first paragraph, as one skilled in the art clearly would not know how to use the claimed invention. The rejection of claim 2 under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite was withdrawn. Therefore, claims 1, 2, 6 and 7 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

For the purposes of Appeal the proposed amendments revising claim 2 will be entered by the Examiner in response to the Final Action mailed on April 28, 2003. Appellants believe that no additional outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode a novel human G protein-coupled receptor. The specification details a number of uses for the presently claimed polynucleotide sequences, including the detection and diagnosis of human diseases such as, *inter alia*, atherosclerosis, heart disease, abnormal blood pressure, cancer, (specification at page 4, lines 6-10). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page 36, line 1-5), particularly using a high throughput "chip" format (specification at page 9, line 24 through page 10, line 10), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions (specification at page 12, line 17-22), determining the genomic structure (specification at page 12, lines 14-17), and in diagnostic assays such as forensic analysis, human population biology and paternity determinations (see, for example, the specification from page 12, line 14-17).

VI. ISSUES ON APPEAL

1. Do claims 1, 2, 6 and 7 lack a patentable utility?
2. Are claims 1, 2, 6 and 7 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1, 2, 6 and 7 Lack a Patentable Utility?

The Final Action first rejects claims 1, 2, 6 and 7 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial utility or a well-established utility, this rejection is maintained in the Advisory Action.

Appellants strongly disagree, as the specification details a number of specific and substantial utilities for the presently claimed polynucleotide sequences, including the detection and diagnosis of human diseases such as *inter alia*, atherosclerosis, heart disease, abnormal blood pressure, cancer, (specification at page 4, lines 6-10). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page 36, line 1-5), particularly using a high throughput "chip" format (specification at page 9, line 24 through page 10, line 10), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions (specification at page 12, line 17-22), determining the genomic structure (specification at page 12, lines 14-17), and in diagnostic assays such as forensic analysis, human population biology and paternity determinations (see, for example, the specification from page 12, line 14-17).

Appellants would like to invite the Board's attention to the fact that a sequence sharing greater than 94% identity at the nucleic acid level with the sequences of the present invention is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third

party scientists *wholly unaffiliated with Appellants* as *Homo sapiens* putative vascular inducible G protein-coupled receptor (VIGR) mRNA (GenBank accession number AF216967; alignment and GenBank report provided in **Exhibit A**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be little question that those skilled in the art would clearly believe that Appellants' sequence is a novel human G protein-coupled receptor, as set forth in the specification as originally filed. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Advisory Action (at page 2, lines 6-7), states that "Neither the specification not the art of record disclose any diseases or conditions associated with the function or expression of the NGPCR protein, therefore there is no "real world" context of use". Appellants' strongly disagree, as the specification details a number of specific and substantial utilities for this the presently claimed polynucleotide sequences, which encode a vascular inducible G protein-coupled receptor (VIGR) were described in the specification(at page 4) as having utility in the detection and diagnosis of human diseases, *inter alia*, atherosclerosis, heart disease and abnormal blood pressure (all of which are vascular indications).

Furthermore, it is well known to the art that novel human G-protein coupled receptors have a well-established utility. This assertion is evidenced by the fact that 60% of these drugs target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. *8*:1605-1648: **Exhibit B**). In addition, Applicants' assertion, that the presently described sequences have specific, credible and well-established utility, is also supported by the fact that multiple millions of dollars are allocated yearly in the identification and targeting of G-protein coupled receptors such as those of present invention. If these molecules did not have well-established utility recognized by those of skill in the art in the pharmaceutical industry, surely those in such a competitive industry would not direct so much of their limited resources towards these molecules.

Further evidence of the physiologic importance of the molecules encoded by the sequences of the present invention is clearly demonstrated by results obtained when a knockout mouse was made in

which the mouse gene encoding the ortholog of SEQ ID NOS: 1 and 2 of the present invention was disrupted by homologous recombination and the knockout mice were subject to a medical work-up using an integrated suite of medical diagnostic procedures designed to assess the function of the major organ systems in a mammalian subject. Disruption of the mouse gene of the present invention and thus elimination of the protein it encodes, resulted in neonatal lethality.

Thus, the skilled artisan would readily appreciate the utilities asserted by Appellants' regarding the role of the proteins encoded by sequences of the present invention in vascular and coronary diseases associated with the provision of a novel human sequence encoding a G-protein coupled receptor (VIGR), involved in vascular disease and which is apparently essential to normal development. Therefore, the present utility rejection must fail. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

The Advisory Action discounts Appellants' assertion regarding the use of the presently claimed polynucleotides on DNA gene chips, based on the position that such a use would allegedly be generic. Further, these Actions seem to be requiring Appellants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Appellants respectfully point out that knowledge of the exact function or role of the presently claimed sequence <u>is not required</u> to track expression patterns using a DNA chip. As set forth in Appellants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications.

Clearly, the claimed sequences provide a <u>specific</u> marker of the gene encoding VIGR and provide a unique identifier of the corresponding gene in the human genome. Such <u>specific</u> markers are targets for discovering drugs that are associated with human kidney disease, such as congenital

nephrotic syndrome. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details at least on page 9, line 24 through page 10, line 10. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit C**), 5,556,752 (**Exhibit D**), 5,744,305 (**Exhibit E**), as well as more recently issued U.S. Patent Nos. 5,837,832 (**Exhibit F**), 6,156,501 (**Exhibit G**) and 6,261,776 (**Exhibit H**).

The Board is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding VIGR, must in themselves be useful. Moreover, the presently described protein (VIGR) provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Additionally, only a small percentage of the genome (2-4%) actually encodes exons, which in turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications. This further discounts the Examiner's position that such uses are "generic". The present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit I**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit J**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome (specification at page 14, lines 9-10), for example mapping the protein encoding regions as described in the specification (page 3, line 26-29) and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequence.

In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Appellants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Applicants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit K**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 25 exons spread non-contiguously along a region of human chromosome 6, which are contained within partially overlapping clones, AL360007.11 and AL033377.2. Thus clearly one would not simply be

able to identify the 25 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

While not reiterated in the Final Office Action, the First Action gave a number of additional reasons for the alleged lack of utility. The First Action stated that Appellants demonstrates neither the function of the protein encoded by SEQ ID NO:1 nor the function of the polypeptide of SEQ ID NO:2. Appellants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). The First Action went on to state that the invention lacks utility because the disclosure provides no guidance as to where the important structural elements of the claimed protein such as the catalytic domain, binding domain and the like are located (the First Action at page 2). This is also misplaced, as it is well established that "an inventor is not required to understand the theory of how his invention works". *Micro Motion, Inc. v. Exac Corp.,* 16 USPQ2d 1001, 1013 (Cal. 1990).

In the Advisory Action, the Examiner maintains the position that "it is commonly known in the art that sequence to function methods of assigning protein function are prone to errors". In support of this position the Examiner had, in the First Office Action, cited Doerks *et al.* (Trends in Genetics *14*:248-250, 1998) for the proposition that sequence-to-function methods of assigning protein function are prone to errors. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional information becomes available for at least one member" (Doerks *et al.*, page 248, paragraph bridging columns 1 and 2, emphasis added). The GPCR family is a well-studied protein family with a large amount of known functional information, exactly the situation that Doerks *et al.* suggests will "simplify" and "avoid the pitfalls" of previous sequence-to-function methods of assigning protein function (Doerks *et al.*, page 248, columns 1 and 2). Thus, instead of supporting the Examiner's position against utility, Doerks *et al.* actually supports Applicants' position that the presently claimed sequences have a substantial and credible utility.

The Examiner next cited Brenner (Trends in Genetics *15*:132-133, 1999) as teaching that "accurate inference of function form homology must be a difficult problem" (Action at page 4). However, this statement is based on the assumption that "if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions" (page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is "an issue solvable by appropriate use of modern and accurate sequence comparison procedures" (page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the "modern and accurate sequence comparison procedures" used by Applicants. Thus, the Brenner article also does not support the alleged lack of utility.

The Examiner finally cites Bork *et al.* (Trends in Genetics *12*:425-427, 1996) as supporting the proposition that prediction of protein function from homology information by software robots (circa 1996) that assign functions to new proteins often assign a function based on the structural similarity of a small domain of the new protein to a small domain of a known protein (Action at page 4). Thus, the Examiner's reliance on Bork *et al.* has the same failing as described above for Doerks *et al.*, specifically, that the GPCR family is well studied and the assumption that Applicants assertion that the present sequences are GPCRs are made on the basis of structural similarity of a small domain of the new protein to a small domain of a known protein. Thus, Applicants assertion that the present sequences are GPCRs are not made on the basis of "structural similarity of a small domain of the new protein to a small domain of a known protein", but rather homology over a large sequence. Thus, Bork *et al.* also does not support the alleged lack of utility for the present invention.

Furthermore, a careful reading of the cited "relevant literature" does not in fact support the concept that function cannot be based on sequence and structural similarity, in contrast many of the examples actually support the use of such methodologies while identifying several areas in which caution should be exercised. These inaccuracies and potential pitfalls can be overcome by a more careful analysis by those of skill in the art. Automatic methods of sequence homology identification was only the staring point for consideration the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (B.S. and Ph.D. level scientists).

These articles are merely examples of a small number of spurious publications that call into doubt the usefulness of bioinformatic predictions and that the PTO has repeatedly attempted to use as a basis to deny the utility of nucleic acid sequences. However, without going into the merits (or lack thereof) of all of the cited articles, Appellants point out that the lack of 100% unanimous agreement on the usefulness of bioinformatic prediction programs is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility. Appellants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. Appellants submit that the overwhelming majority of those of skill in the relevant art would **believe** bioinformatic prediction to be a powerful and useful tool, as evidenced by hundreds if not thousands of journal articles.

Rather, the question of utility is a straightforward one. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the

assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d

1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Additionally, methods similar to those of the present invention were used to identify the GPCR of issued U.S. Patent 6,043,052. Issued U.S. Patents are presumed to be valid and to meet the requirements of 35 U.S.C. §§ 101, 102, 103 and 112, specifically, that they have utility, are novel, non-obvious, are enabled, meet the written description requirements and particularly point out and distinctly claim the invention. Therefore, the Applicants' assertion that the described GPCR is in fact a GPCR is supported by issued U.S. Patent 6,043,052, as well as the plethora of other GPCR patents that the office has issued. For example, the specific and substantial utility of human GPCRs is evidenced by the fact that they are the subject of the above mentioned U.S. Patent No. 6,043,052 which discloses polynucleotides encoding a novel GPCR and U.S. Patent Nos. 5,891,646 and 6,110,693, both of which disclose and claim methods for detecting GPCR activity *in vivo* and *in vitro*, methods for assaying GPCR activity, and methods of screening for GPCR ligands, GPCR kinase activity, components that interact with GPCR regulatory processes and constructs useful in such methods. The issuance of these U.S. patents clearly indicates that GPCR polynucleotides have utility and that such utilities were sufficiently specific and substantial to warrant the issuance of U.S. patents directed to methods used to identify and characterize GPCRs. The teachings of these patentable disclosures are directly applicable to the present invention (GPCR polynucleotides) and are evidence that those skilled in the art recognize the specific and substantial utility of GPCRs. In light of the issuance of U.S. Patent No. 6,043,052 on polynucleotides encoding a novel GPCR, Applicants respectfully submit that the present application, which also describes polynucleotides encoding a novel GPCR, describes an invention with specific and substantial utility fully compliant with 35 U.S.C. § 101.

Finally, with regards to the issue of due process, while Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO.

Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit L**), 5,654,173 (**Exhibit M**), and 5,552,281 (**Exhibit N**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit O**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants are aware that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Given the rapid pace of development in the biotechnology arts, it is difficult for the Appellants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Appellants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1, 2, 6 and 7 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1, 2, 6 and7 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1, 2, 6 and 7 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in **Section VIII(A)** concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana*, *supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1, 2, 6 and7 have been shown to have "a specific, substantial, and credible utility", as detailed in **Section VIII(A)** above, the present rejection of claims 1, 2, 6 and 7 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1, 2, 6 and 7 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. An isolated nucleic acid molecule containing the nucleotide sequence described in SEQ ID NO: 1.

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

6. An expression vector comprising an isolated polynucleotide encoding the amino acid sequence presented in SEQ ID NO: 2.

7. A cell comprising the expression vector of Claim 6.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1, 2, 6 and 7 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

September 2, 2003
Date

Reg No 40162
Peter G Setterian

Lance K. Ishimoto Reg. No. 41,866
Agent For Appellants

LEXICON GENETICS INCORPORATED
(281) 863-3333

Customer # 24231